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Cable "TUMED"

March 11, 1989

Dr. Robert A. Goldstein
Chief, Clinical Immunology
and Immunopathology Branch
National Institute of Allergy
and Infectious Diseases
Westwood Building, Room 757
Bethesda, Maryland 20892

Re: R01 AI24003-04

Dear Dr. Goldstein:

I learned yesterday that my renewal application, "Mechanisms of Oxidative Toxicity," received a priority score of 300 and thus will not be funded. For the reasons given below, I feel that my application received an unfair review, and I should like to request that it be reviewed again in June at the next cycle of the Microbial Physiology and Genetics Study Section, which was responsible for its initial review and which I believe would be more qualified to evaluate my progress.

The original application was based on preliminary data indicating the involvement of free radical mechanisms in the action of hypochlorous acid on nucleotides and received a priority score of 142. A request for a supplement (AI24003-02S1), although not funded, received a priority score of 147. The supplement was based on the same type of work proposed in my present renewal. The disparity in scores alone suggests that something is not right.

Aside from scores, the fact remains that progress on this grant has been excellent. Such progress is embodied in the eleven articles that appeared or were submitted up to the time of the review. Copies of these items were appended to the grant, and a listing is attached to this letter. Four additional manuscripts (not listed) are in preparation. The poor priority score that the grant received represents a failure to recognize the progress that has been made. What is more important, it ignores the promise of progress to come, especially since the difficult, initial discoveries have now been made.

I attribute the present poor score to the fact that the renewal application was not sent to the Study Section that originally reviewed it, and I share the blame for this as I did receive notificiation of the Study Section change. However. I did not realize its full implication until a month ago, when it was too late to effect a change. I suspect that the review was strongly influenced by a biochemist member of the

Bacteriology and Mycology Study Section who is a competitor in the field of hypochlorous acid chemistry and who may have given a biased evaluation. Of course, verification of this suspicion will have to await examination of the Summary Statement, and I will be quick to apologize if I am wrong about this.

In the meantime, I should like you to consider my request that my application be reevaluated and that the Summary Statement be sent to me in time to prepare a detailed rebuttal.

Sincerely yours,

Carl Bernofsky, Ph.D.
Research Professor

cc: Dr. William C. Branche, Jr.

Publications

These papers appeared or were submitted during the period covered by the previous grant period.

1. Bernofsky, C., and O'Dea, S. W. (1986), Nucleotide Modification, a Radical Mechanism of Oxidative Toxicity, Free Radical Res. Commun., 2, 129-136.

2. Bernofsky, C. (1987), The Nature and Biochemical Significance of Compounds Derived from Pyridine Nucleotides, Coenzymes and Cofactors, Vol. 2B (Dolphin, D., Poulson, R., and Avramović, O., eds.), John Wiley & Sons, New York, pp. 105-172.

3. Bernofsky, C., Strauss, S. L., and Hinojosa, O. (1987), Binding of Hypochlorite-Modified Adenosine 5'-Monophosphate (AMP) to Protein and Nucleic Acid and Its Possible Role in Cytotoxicity, Biochem. Arch., 3, 95-101.

4. Bernofsky, C., Sono, M., O'Dea, S. W., and Olavesen, E. Y. (1987), Isolation and Some Properties of a Free Radical Hypochlorite-Oxidation Product of Adenosine 5'-Monophosphate (AMP), Biochem. Arch. 3, 147-155.

5. Bernofsky, C., and Strauss, S. L. (1987), Hypochlorite-Mediated Binding of Adenosine 5'-Monophosphate to Nucleic Acid and Its Possible Role in Carcinogenesis, Biochem. Arch., 3, 431-435.

6. Bernofsky, C., Olavesen, E. Y., Felix, C. C., and Kalyanaraman, B. (1988), Evidence for a Hydroperoxyl Radical from Hypochlorite-Modified Adenosine 5'-Monophosphate (AMP), Biochem. Arch., 4, 103-107.

7. Bernofsky, C., and Strauss, S. L. (1988), Evidence for the Formation of Hypochlorite-Modified Adenosine by Activated Guinea Pig Polymorphonuclear Leukocytes, Biochem. Arch., 4, 349-355.

8. Bernofsky, C., and Strauss, S. L. (1989), Evidence that Incorporation of Hypochlorite-Modified Adenosine into Acid-Insoluble Products is Not the Result of Poly(ADP-Ribose) or DNA Synthesis in Activated Guinea Pig Polymorphonuclear Leukocytes, Biochem. Arch., 5, 11-18.

9. Bernofsky, C., and Strauss, S. L., Oxygen Requirement for Incorporation of Adenosine into Acid-Insoluble Products by Activated Guinea Pig Polymorphonuclear Leukocytes, Biochem. Arch. (In Press).

10. Bernofsky, C., Bandara, B. M. R., and Hinojosa, O., Spin-Trapping the Adenosine Free Radical (Submitted).

11. Bernofsky, C., Bandara, B. M. R., and Hinojosa, O., Electron Spin Resonance Studies of the Reaction of Hypochlorous Acid with 5,5-Dimethyl-1-Pyrroline-N-Oxide (Submitted).